# Health-Related Quality of Life and Its Contributors According to a Preference-Based Generic Instrument in Cirrhosis

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**It is essential to determine contributors around impairment in health-related quality of life (HRQoL) in patients with cirrhosis aiming at improving health care and therapeutic strategy. Studies simultaneously incorporating disease severity based on biochemical parameters and other physical/psychological effects (i.e., sleep disturbance and frailty) are heterogeneous and the subject of the present study. We analyzed and compared HRQoL, using the EuroQol Group 5 Dimension (EQ-5D) questionnaire and the utility index retrieved, in patients with cirrhosis and across groups stratified by sleep disturbance or frailty phenotype. Sleep disturbance and frailty were determined by the Pittsburgh Sleep Quality Index (PSQI) and Frailty Index, respectively. Multiple linear regression was implemented to clarify contributors of poor HRQoL. In this cohort of 227 patients with mean age of 61.7 years and 47.2% male, more than half of the study population represented impairment in HRQoL in at least one domain, according to EQ-5D. Furthermore, sleep disturbance and frailty have proved to be independently associated with poor HRQoL in two separate regression models, whereas conventional scoring systems such as Child-Pugh classification and Model for End-Stage Liver Disease are not closely relevant. Intriguingly, not all health domains within EQ-5D correlated well with PSQI and Frailty Index, with the exception of usual activities. Pain and anxiety/depression were the most frequently affected HRQoL domains even in patients without sleep disturbance or frailty. *Conclusion:* Impaired HRQoL is prevalent in patients with decompensated cirrhosis. Sleep disturbance and frailty are independently associated with poor HRQoL. It is imperative to timely intervene with these symptoms and deliver tailored health care. (*Hepatology Communications* 2022;6:610-620).**

Patients with cirrhosis often experience impairment in health-related quality of life (HRQoL), while this phenotypic perturbation is more profound in decompensated conditions.[1] More recently, a prospective cohort study conducted by Kok et al. also clarified that poor HRQoL is independently related to increased mortality and unplanned hospitalization in patients with cirrhosis.[2] However, most literature in the realm of hepatology has only taken into account ameliorating disease severity or delaying its progression, referring to better biochemical parameters and prolonged survival time.[3] In actuality, it is essential to implement comprehensively holistic evaluation pertaining to HRQoL both in daily practice

*Abbreviations: BMI, body mass index; EQ-5D, EuroQol Group 5 Dimension; EQ-5D-3L, three levels of each EQ-5D domain; HE, hepatic encephalopathy; HGS, handgrip strength; HRQoL, health-related quality of life; MELD, Model for End-Stage Liver Disease; PSQI, Pittsburgh Sleep Quality Index.*

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and clinical trial, as this outcome is readily available and commonly present in cirrhosis at different disease stages.[4,5] Furthermore, another benefit to assess this patient-reported outcome leads to the development of effective therapeutic strategies and delivery of patient-centered health care. Although the clinical significance and relevance of HRQoL have attracted substantial attention in the medical field, there is still lacking of consistency around contributors of impaired HRQoL and their independence to conventional scoring systems such as Child-Pugh classification or Model for End-Stage Liver Disease (MELD).[6] Notably, it is critical to identify contributors precipitating poor HRQoL with the purpose of facilitating the priority of management. On the other hand, it is tempting to mitigate HRQoL by modifying its core components, including physical and psychological dimensions.

The assessed constructs with regard to HRQoL consist of generic/preference-based and disease-specific tools. Generally speaking, it is valid and reproducible to adopt both instruments in terms of study design, and practical convenience in the context of liver disease.[7] The EuroQol Group 5 Dimension (EQ-5D) is designated as one of the most preferred tools for quantifying HRQoL in the general population and in a pathological entity, namely, chronic liver disease where its validity has been widely affirmed.[8-13] The EQ-5D questionnaire covers a broad array of health issues, including mobility, self-care, usual activities, pain and anxiety/depression, and subsequently generating a utility index. Of note, it is advantageous to compare the retrieved utility index among different studies in case of lacking control groups or available population norms.[11] In addition, one can also obtain the quality-adjusted life-year by multiplying utility index with time period that an individual maintains in certain health state, which is useful for further estimation regarding cost-utility analyses.[14] After bibliographic review of the current literature, we found there are limited data looking at the clinical relevance of EQ-5D alongside a utility index in patients with cirrhosis and their relationship with impacting factors, such as sleep disturbance and frailty.[2] Another problem arises from the ambiguous studies that look into the HRQoL of patients with end-stage liver disease, predominantly concentrating on liver transplant recipients, not in patients with possible cirrhosis with decompensation.[7,15] Accordingly, we aimed to (1) dissect the holistic status of impairment in HRQoL according to EQ-5D in our well-established cohort of patients with decompensated cirrhosis; (2) identify independent contributors relevant to poor HRQoL, taking consideration of both underlying disease severity (laboratory findings and symptoms) and EQ-5D scores; and (3) clarify which HRQoL domains are most affected by these detrimental factors and whether there is variability across different EQ-5D domains.

# Patients and Methods

## STUDY POPULATION

We consecutively, prospectively recruited hospitalized patients aged 18 years and older at the Department of Gastroenterology and Hepatology, Tianjin Medical

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University General Hospital (TJMUGH) from 2019 to 2021. The diagnosis of liver cirrhosis was based on medical history, endoscopic appearance, laboratory results, imaging data, as well as pathological findings. Additionally, the presence of cirrhosis-associated complications like esophagogastric varices, variceal bleeding, ascites and hepatic encephalopathy (HE), was recorded. The exclusive criteria were closely adherent to our previous publication and briefly stated as follows: (1) present with concomitant acute-on-chronic liver failure on index admission; (2) present with sever HE, preventing the participant from finishing the questionnaire (as recognized by a time to finish a numbers connection test >120 seconds); (3) present with concurrent intrahepatic or extrahepatic malignancies; and (4) refusal to follow-up visits. This study was preformed according to the Declaration of Helsinki and was approved by the ethics committee of TJMUGH. All patients provided written, informed consent at enrollment.

## QUESTIONNAIRE SURVEY REGARDING SLEEP DISTURBANCE, FRAILTY, AND HRQOL

The detail with respect to the Pittsburgh Sleep Quality Index (PSQI) and Frailty Index has been explicitly depicted in our previous work.[16] However, the EQ-5D refers to a well-established quality-of-life tool that is generic and preference-based.[17] This questionnaire consists of a descriptive system with five separate dimensions (i.e., mobility, self-care, usual activities, pain, and anxiety/depression). A total number of 243 ($3^5$) possible disparate health states can be calculated on account of the three levels of each domain (EQ-5D-3L). It is essential to obtain a single value for each of these disparate health states, with the purpose of assessing HRQoL. Accordingly, the EQ-5D utility index results from a country-specific value setting that has been previously established using the trade-off method and exhibits the preferences of the particular country. Because a representative validated Chinese specific value setting is unavailable, we calculated the utility index for our study population according to the Japanese population value setting, while taking consideration the comparability between these two East Asia countries.[18] Specifically, a negative utility index value represents the situation in which patients may evaluate their health state worse than death. The value "1" equals the best health status, and a higher index value indicates a better HRQoL. All questionnaires were asked to perform within 48 hours of hospitalization.

## DEMOGRAPHIC AND BIOCHEMICAL PARAMETERS

The patients' characteristics including demographic feature, clinical manifestation, and laboratory data were retrieved upon hospitalization. One can find detailed information in our previous work.[16]

## STATISTICAL ANALYSIS

The descriptive statistics are shown as mean ± SD or median (interquartile range), and simple frequency and percentage for categorical data as appropriate. Continuous data were compared using an independent Student *t* test or the Mann-Whitney U test for variables without normal distribution. Categorical variables were compared by Pearson $\chi^2$ test or Fisher's exact test. The Spearman's correlation coefficient ($r_s$) was calculated between the EQ-5D utility index and single dimension of the EQ-5D, and the PSQI/Frailty Index. Contributors of impaired HRQoL were calculated by linear regression analyses, with the EQ-5D utility index as the dependent variable. The variables' age, body mass index (BMI), PSQI, handgrip strength (HGS), Frailty Index, ascites, HE, Child-Pugh score, MELD, platelet-to-lymphocyte ratio, albumin, and sodium were included as independent variables in two separate models. We incorporated a predictive variable at the level of $P < 0.1$ in simple regression analyses, to enter into multiple regression analyses. The resulting standardized $\beta$ coefficient with 95% confidence interval and *P* value are shown. The threshold for statistical significance is set at $P < 0.05$. All statistical analyses were performed using SPSS 21.0 (IBM, New York, NY) and GraphPad Prism 8.0.1 (La Jolla, CA).

# Results

## PATIENTS

During the study period, a total of 227 hospitalized patients with cirrhosis and cirrhosis-associated complications were consecutively recruited. The

**TABLE 1. BASELINE CHARACTERISTICS IN THE COHORT OF PATIENTS WITH DECOMPENSATED CIRRHOSIS**

| | Total (n = 227) |
|---|---|
| Age (years) | 63 (57-68); 61.7 ± 9.9 |
| Gender, n (%) | |
| Male | 107 (47.1) |
| Female | 120 (52.9) |
| Ethnicity/race, n (%) | |
| Asian | 227 (100.0) |
| BMI (kg/m$^2$) | 23.4 (20.2-26.7); 23.8 ± 4.6 |
| Etiology, n (%) | |
| Viral infection | 68 (30.0) |
| Alcohol/NAFLD | 50 (22.0) |
| AILD/cholestatic | 68 (30.0) |
| Cryptogenic | 41 (18.1) |
| Esophagogastric varices, n (%) | 171 (75.3) |
| Ascites*, n (%) | 134 (59.0) |
| Variceal bleeding, n (%) | 78 (34.4) |
| History of HE, n (%) | 17 (7.5) |
| Child-Pugh score | 7 (6, 9) |
| Child-Pugh classification, n (%) | |
| A† | 73 (32.2) |
| B/C | 154 (67.8) |
| PSQI | 7 (4,11) |
| Frailty Index | 0.13 (0.06, 0.26) |
| MELD | 9.0 (6.2, 11.8) |
| Na (mmol/L) | 140 (138, 142) |

Note: Data are presented as the mean ± SD, median (interquartile range), or percentage of patients (%). Percentages may not add up to 100% because of rounding.
Abbreviations: NAFLD, nonalcoholic fatty liver disease; AILD, autoimmune liver disease.
*Of those, 11 patients presented refractory ascites, 33 presented ascites on ultrasound, and 90 presented ascites controlled on diuretics.
†Within Child-Pugh classification A, 55 patients presented prior variceal bleeding alone, 14 patients presented controllable ascites alone, and 4 patients presented both complications.

baseline characteristics of the study population are given in Table 1. Mean age was 61.7 years, and 47.1% were male. The etiologies of cirrhosis were due to chronic virus hepatitis in 68, autoimmune/cholestatic liver disease in 68, and alcohol-associated liver disease/nonalcoholic fatty liver disease in 50 patients. The presence of major cirrhosis-associated complications include esophagogastric varices in 171, ascites in 134, variceal bleeding in 78, and HE in 17, respectively. Of those, 32.2% were categorized into Child-Pugh class A and 67.8% into Child-Pugh class B/C. Median MELD was 9.0 points upon hospitalization.

## DISTRIBUTION OF EQ-5D PROFILE

First, we intend to illustrate global HRQoL state of the study population by displaying the EQ-5D-3L distribution in Fig. 1. The proportions of patients with cirrhosis reporting some or extreme complaints in different domains were 15.0% in self-care, 18.5% in usual activities, 18.5% in mobility, 31.3% in anxiety/depression, and 31.7% in pain. On the basis of our patient cohort, 44.9% (n = 102) of the subjects with decompensated cirrhosis reported no complaint in any health domain, 19.4% (n = 44) represented no complaints in four domains, 19.0% (n = 43) had no complaints in three domains, 6.6% (n = 15) in two domains, and 4.4% (n = 10) in single domain, whereas 5.7% (n = 13) reported complaints in all health domains.

## CONTRIBUTORS OF POOR HRQoL IN PATIENTS WITH DECOMPENSATED CIRRHOSIS

Multiple adjustments for independent contributors of HRQoL are found in Table 2, with Child-Pugh score–based and MELD-based models analyzed separately. In the Child-Pugh score model, higher PSQI ($\beta$ coefficient = −0.198; $P$ = 0.005) and Frailty Index ($\beta$ coefficient = −0.418; $P$ < 0.001) were independently associated with low EQ-5D utility index, with Child-Pugh dropping out of the model. Similarly, higher PSQI ($\beta$ coefficient = −0.216; $P$ = 0.003) and Frailty Index ($\beta$ coefficient = −0.392; $P$ < 0.001) were also independently associated with low EQ-5D utility index, with MELD dropping out of the model.

## CORRELATION ANALYSES BETWEEN THE EQ-5D AND SLEEP DISTURBANCE/FRAILTY PHENOTYPE

The correlation analyses between the overall EQ-5D utility index and the PSQI gave rise to a significantly negative Spearman's coefficient $r_s$ = −0.437 ($P$ < 0.001), showing a correlation between both of those parameters. Domains with the strongest correlation with the PSQI were usual activities ($r_s$ = 0.346, $P$ < 0.001) and anxiety/depression ($r_s$ = 0.335, $P$ < 0.001), whereas only weak correlations occurred in the domains self-care ($r_s$ = 0.260, $P$ < 0.001) and mobility ($r_s$ = 0.287, $P$ < 0.001) (Fig. 2).

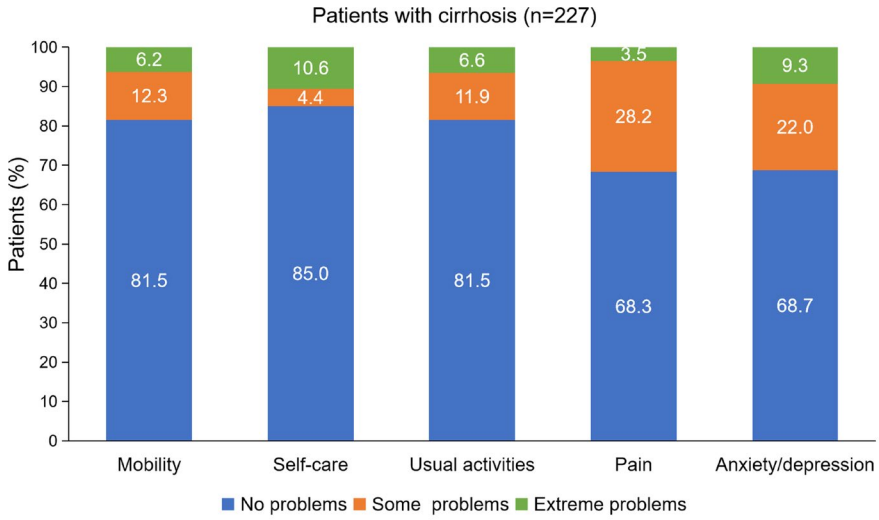


**FIG. 1.** Distribution of the EQ-5D profiles in the cohort of patients with decompensated cirrhosis (n = 227). The EQ-5D questionnaire consists of five health domains: mobility, self-care, usual activities, pain, and anxiety/depression. Each of these dimensions consist of three levels: no, some, or extreme problems. The distribution of the profiles of patients with cirrhosis with decompensation according to each health domain is shown.

**TABLE 2. SIMPLE AND MULTIPLE LINEAR REGRESSION ANALYSES TO ASSESS ASSOCIATIONS BETWEEN THE FOLLOWING VARIABLES AND EQ-5D UTILITY INDEX**

| | Simple Regression Analysis | | | Multiple Regression Analysis, Model 1* | | | Multiple Regression Analysis, Model 2* | | |
|---|---|---|---|---|---|---|---|---|---|
| Variable | *β* | 95% CI | *P* | *β* | 95% CI | *P* | *β* | 95% CI | *P* |
| Age (years) | –0.154 | –0.286, –0.024 | 0.021 | 0.020 | –0.101, 0.135 | 0.778 | –0.001 | –0.125, 0.122 | 0.986 |
| Gender | –0.044 | –0.175, 0.087 | 0.511 | | | | | | |
| BMI (kg/m$^2$) | 0.204 | 0.067, 0.309 | 0.002 | 0.108 | –0.025, 0.210 | 0.121 | 0.131 | –0.008, 0.237 | 0.068 |
| PSQI | –0.388 | –0.509, –0.267 | <0.001 | –0.198 | –0.286, –0.053 | 0.005 | –0.216 | –0.305, –0.066 | 0.003 |
| HGS | 0.212 | 0.066, 0.341 | 0.004 | 0.085 | –0.049, 0.194 | 0.243 | 0.070 | –0.067, 0.186 | 0.351 |
| Frailty Index | –0.511 | –0.624, –0.398 | <0.001 | –0.418 | –0.524, –0.240 | <0.001 | –0.392 | –0.514, –0.216 | <0.001 |
| Ascites | –0.134 | –0.266, –0.002 | 0.046 | | | | –0.072 | –0.184, 0.059 | 0.310 |
| HE | –0.202 | –0.335, –0.072 | 0.003 | | | | –0.004 | –0.146, 0.137 | 0.952 |
| Child-Pugh score | –0.142 | –0.275, –0.011 | 0.034 | 0.059 | –0.074, 0.178 | 0.416 | | | |
| PLR | –0.202 | –0.332, –0.072 | 0.002 | –0.019 | –0.143, 0.107 | 0.776 | –0.003 | –0.129, 0.124 | 0.966 |
| Albumin (g/L) | 0.122 | –0.008, 0.253 | 0.066 | | | | –0.063 | –0.178, 0.071 | 0.396 |
| ALT (U/L) | 0.023 | –0.108, 0.154 | 0.732 | | | | | | |
| ALP (U/L) | –0.061 | –0.192, 0.070 | 0.363 | | | | | | |
| Total bilirubin (μmol/L) | –0.039 | –0.170, 0.093 | 0.561 | | | | | | |
| MELD | –0.115 | –0.246, 0.016 | 0.086 | | | | –0.046 | –0.177, 0.095 | 0.550 |
| Na (mmol/L) | 0.251 | 0.124, 0.378 | <0.001 | 0.065 | –0.072, 0.198 | 0.357 | 0.048 | –0.094, 0.188 | 0.513 |

Note: Results represent the correlation parameter (*β*), its 95% CI, and the associated *P* value. Multiple regression analysis model 1: age, BMI, PSQI, HGS, Frailty Index, Child-Pugh score, PLR, and sodium. Multiple regression analysis model 2: age, BMI, PSQI, HGS, frailty, ascites, HE, PLR, albumin, MELD, and sodium.
Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; CI, confidence interval; PLR, platelet-to-lymphocyte ratio.

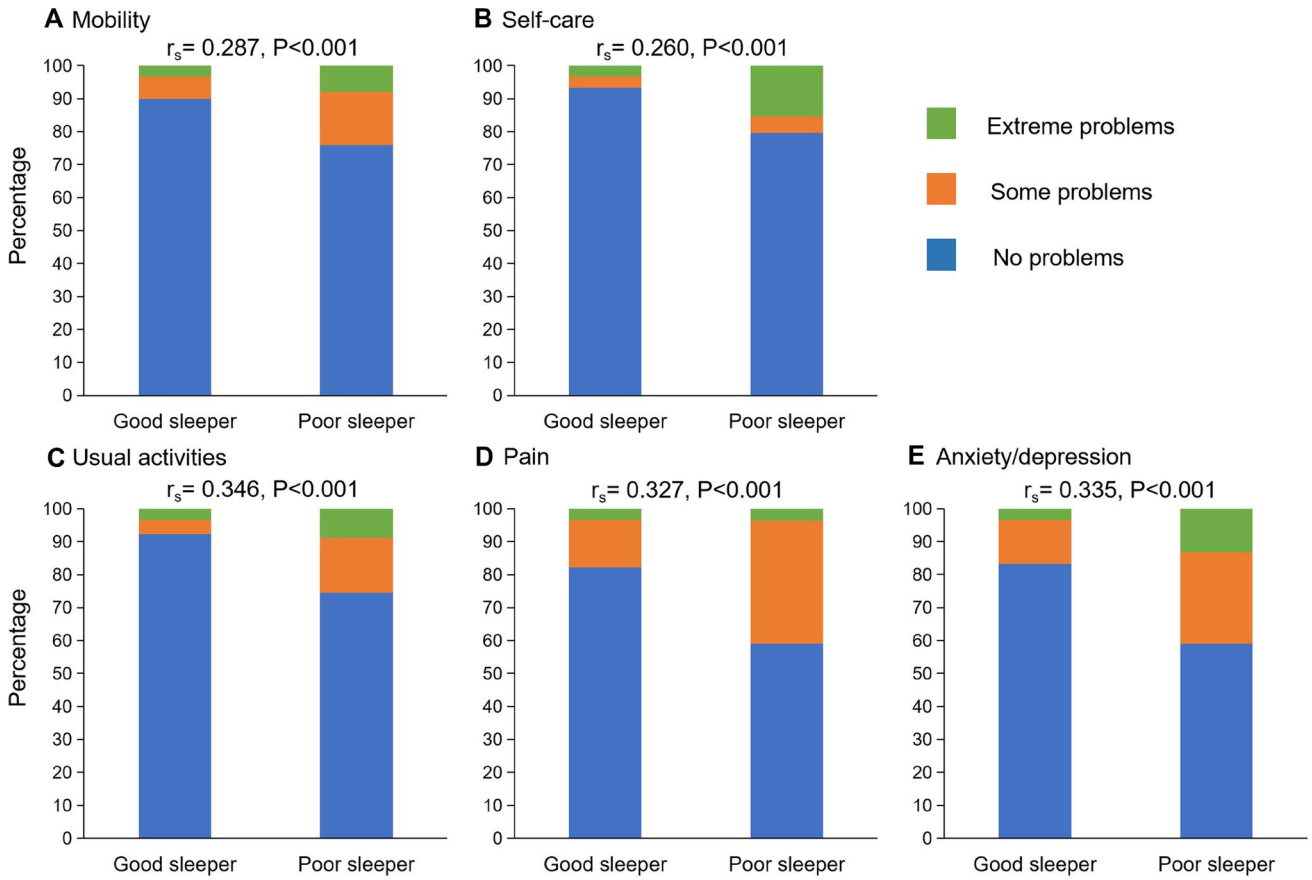


**FIG. 2.** Correlation analyses between each domain of the EQ-5D and PSQI score. Correlation analyses between the following domains: mobility (A), self-care (B), usual activities (C), pain (D), and anxiety/depression (E).

Within the correlation between the overall EQ-5D utility index and the Frailty Index, a significantly negative Spearman's coefficient $r_s$ = −0.416 ($P$ < 0.001) was also observed. Higher utility index values (reflecting better HRQoL) were associated with lower Frailty Index values. Domains with the strongest correlation with the Frailty Index were usual activities ($r_s$ = 0.570, $P$ < 0.001) and self-care ($r_s$ = 0.526, $P$ < 0.001), whereas no correlation occurred in the domains of pain ($r_s$ = 0.113, $P$ = 0.189) or anxiety/depression ($r_s$ = 0.073, $P$ = 0.395) (Fig. 3)

## COMPARISON OF EQ-5D PROFILES IN ACCORDANCE WITH SLEEP DISTURBANCE AND FRAILTY PHENOTYPE

Next, we intend to clarify which HRQoL domains are most influenced according to sleep disturbance or frailty categories. When stratified by PSQI, a significantly higher proportion of patients with poor sleep quality (PSQI ≥ 6) had poor HRQoL across all EQ-5D domains as compared with good sleeper (PSQI < 6). Pain and anxiety/depression were most affected, with 40.9% of the cohort reporting some or extreme problems with pain and 40.9% of the cohort reporting some or extreme problems with anxiety/depression (Fig. 4 and Supporting Table S1). Notably, although to a smaller degree than poor sleeper group, patients with cirrhosis and good sleep quality also experienced a marked burden in domains pertained to pain (17.8%) and anxiety/depression (16.7%).

When stratified by Frailty Index, we also observed a significantly higher proportion of patients with frailty phenotype (Frailty Index > 0.38) as compared with non-frailty across all EQ-5D domains. Within multidimensional frailty, usual activities and self-care appeared to be most influenced, with 69.2% of

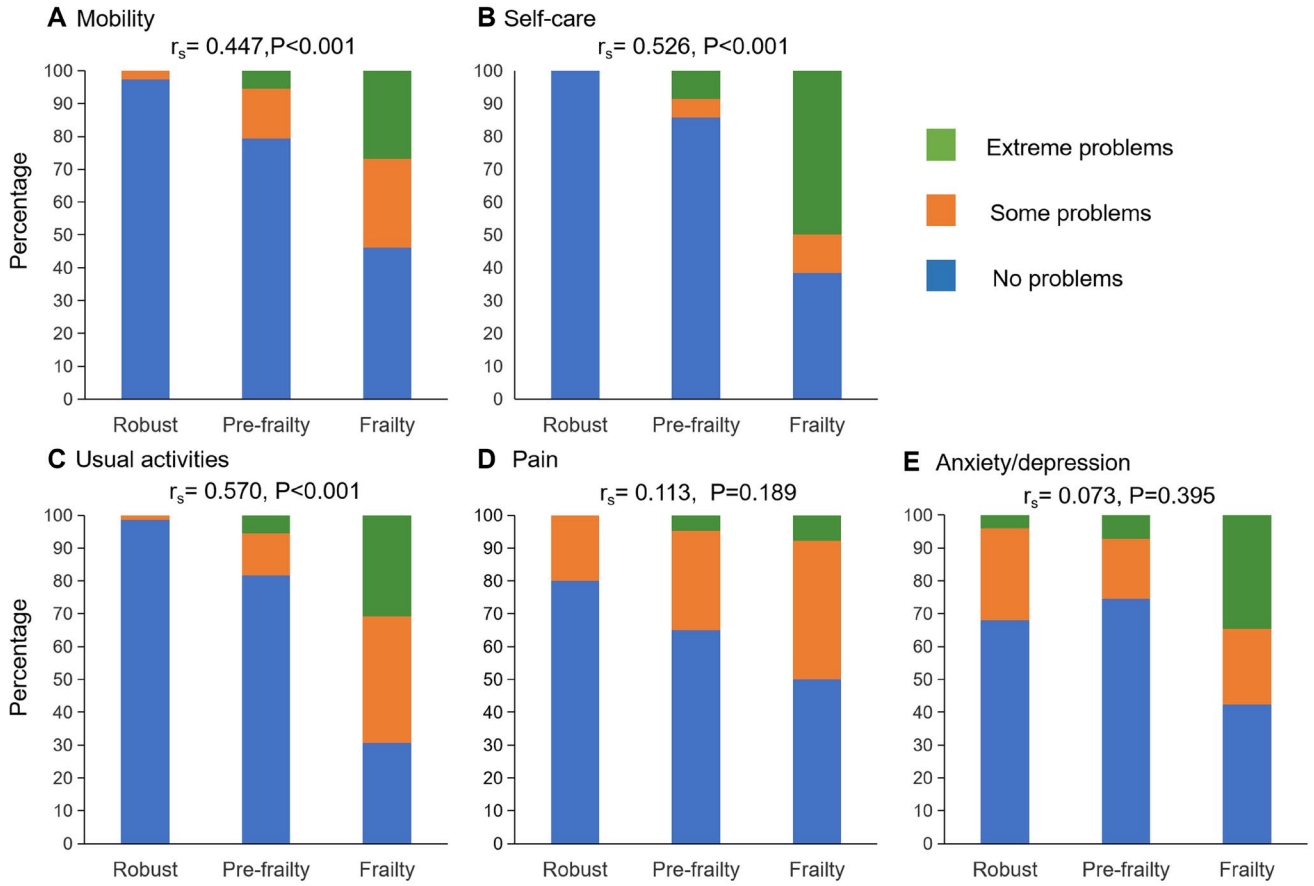


**FIG. 3.** Correlation analyses between each domain of the EQ-5D and Frailty Index. Correlation analyses between the following domains: mobility (A), self-care (B), usual activities (C), pain (D), and anxiety/depression (E).

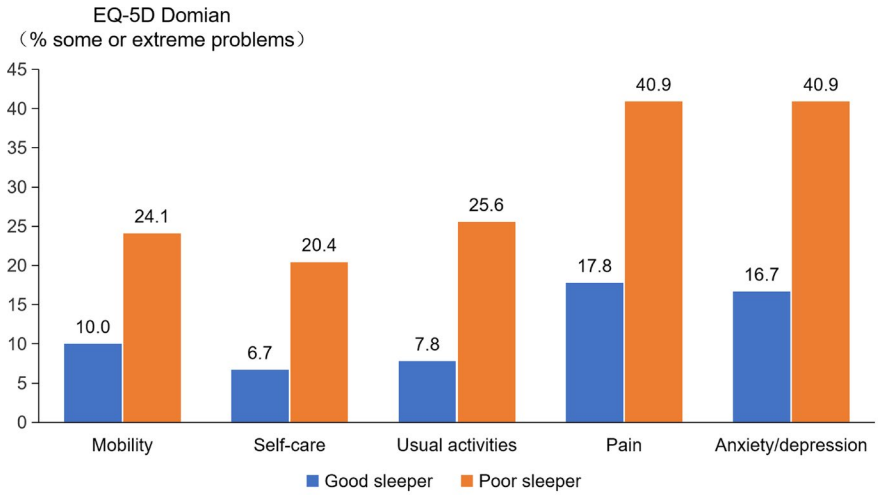


**FIG. 4.** EQ-5D domains stratified by sleep disturbance according to PSQI (good sleeper, PSQI < 6; poor sleeper, PSQI ≥ 6).

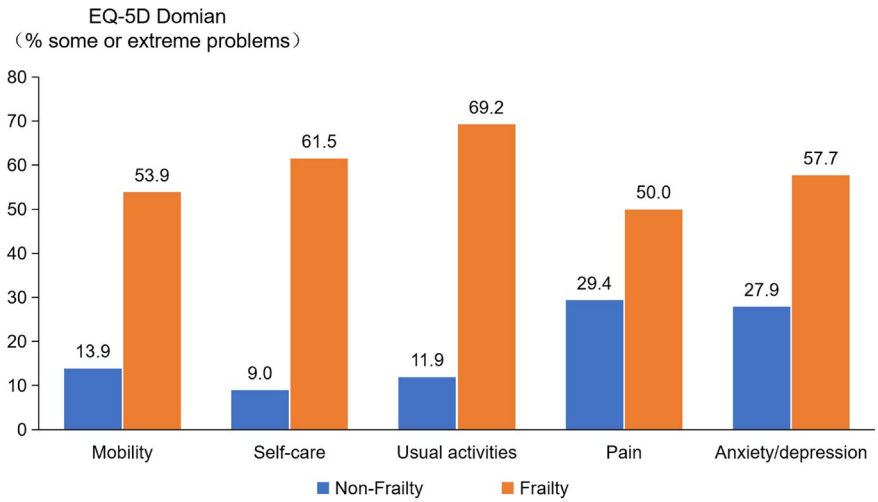


**FIG. 5.** EQ-5D domains stratified by frail phenotype according to Frailty Index (non-frailty, Frailty Index ≤ 0.38; frailty, Frailty Index > 0.38).

the cohort reporting some or extreme problems with usual activities and 61.5% of the cohort reporting some or extreme problems with self-care (Fig. 5 and Supporting able S2). More specifically, patients with cirrhosis representing non-frailty also had a substantial burden in pain (29.4%) and anxiety/depression (27.9%).

# Discussion

In this prospective study, we found that more than half the patients with decompensated cirrhosis represent impairment in HRQoL, at least in one dimension, according to a generic patient-reported instrument (i.e., EQ-5D). Furthermore, sleep disturbance and frailty have proven to be independently associated with poor HRQoL, whereas conventional scoring systems such as Child-Pugh classification and MELD are not closely relevant. Intriguingly, not all health domains within EQ-5D correlated well with PSQI and Frailty Index with the exception of usual activities. Moreover, pain and anxiety/depression appeared to be the most frequently affected HRQoL domains even in patients without sleep disturbance or frailty. It is tempting to timely intervene with these symptoms and deliver tailored health care.

Cirrhosis, characterized by the histopathological development of liver fibrosis, represents a terminal pathway in patients with chronic liver damage due to various etiologies.[19] Alongside persistent and progressive liver injury, this disease may advance into end-stage liver disease (i.e., decompensated cirrhosis with major complications). The 5-year mortality is approximately 85% without liver transplantation when decompensation has occurred.[20] Mounting evidence has implicated that patients with end-stage liver disease encounter physical, psychosocial, as well as financial problems.[21] More recently, a meta-analysis by Peng et al. found that decompensation results in significant worsening of HRQoL in patients with cirrhosis.[7] Furthermore, the most frequently reported symptoms included pain, sleep disturbance, and psychological symptoms (i.e., anxiety/depression). Results from our study corroborate with the aforementioned papers in emphasizing that a remarkable proportion of patients with decompensated cirrhosis experience problems surrounding HRQoL; specifically, 55.1% of the study population exhibited abnormalities in at least one subdomain within EQ-5D. It was particularly striking that more than 10% of participants (n = 23) reported complaints in three or more domains. Taken together, it is crucial to early detect, consecutively monitor, and timely manage these abnormal health states aiming at HRQoL improvement.

Given the high prevalence and heavy burden of impaired HRQoL in cirrhosis, attempts have been made to orchestrate treatment algorithm

and care trajectory. For instance, the American Gastroenterological Association recently updated their clinical practice on palliative care management in cirrhosis[22] and recommended a more comprehensive assessment of data around comorbidities, frailty, functional status, and other issues, as the potential for improvement in addition to etiological therapy. This is the case for population-based prognostic scores such as MELD and Child-Pugh classification, embracing recognized limitations when applied to individual patients. This was certainly reflected in our investigation, in which frailty and sleep disturbance remained independently associated with impairment in HRQoL; Child-Pugh classification or MELD dropped out the multiple adjustment model. Actually, the predictive capability of disease severity indices appears to be heterogeneous. Rabiee et al. addressed that MELD and Child-Pugh classification are closely associated with poor HRQoL in only 49% and 69% of studies, respectively, while sleep and frailty were closely associated in 100% and 80% of the research.[3] The disparities among those studies are in part attributed to different methods and measurements used for evaluating HRQoL.

In our study, we observed a relatively high percentage of problems in the pain and anxiety/depression domains even in patients without sleep disturbance or frailty. Accumulating evidence has suggested that pain is one of the most reported complaints, with a prevalence ranging from 30% to 79%.[23-26] Specially, Madan et al. showed that 90% of 108 subjects with end-stage liver disease were prescribed medication for pain.[27] On the other hand, the presence of psychological symptoms like depression and anxiety are also prevalent in the context of cirrhosis.[7] Collectively, it is critical to provide more information and data on the impact of versatile physical and psychological factors in HRQoL assessed by EQ-5D, taking into consideration recommending EQ-5D as a significant tool to evaluate the value of health care by health technology assessment national agency.[28]

This study has limitations. First, we chose to use EQ-5D-3L in the current study, taking into consideration the ease and simplicity of this questionnaire. In fact, attempts have been made over the past two decades to improve sensitivity by creating a new version of the EQ-5D-5L questionnaire.[29] Second, we cannot assure whether our findings are readily generalizable to other populations with cirrhosis, as this is single-center evidence. Therefore, further studies enrolling patients from multiple centers are warranted. Third, any association revealed between HRQoL and other factors is supposed to be interpreted with caution, especially with regard to causality. Finally, although our cohort is sizable (n = 227), there are no biochemical indices that emerge as an independent contributor of HRQoL. This may need to be investigated in a cohort with even larger numbers.

Herein we acknowledge several strengths of the present study. First, it has been reported that patients with cirrhosis show more tendency to undergo regular surveillance and higher adherence to follow-up visits.[30] In providing a comprehensive depiction of HRQoL information in patients with decompensated cirrhosis, we were able to deliver specific management targeting both mental as well as physical domains from the patient's perspective. Second, we affirmed that sleep disturbance and multidimensional frailty are contributors of poor HRQoL, regardless of liver function reserve in two regression models. These findings appear to be meaningful in clinical practice, as it is common to overlook surrogate outcomes such as patient-reported quality of life by cirrhosis providers. As a matter of fact, it has been questioned whether interventions prolonging survival truly improve HRQoL in patients with malignancies. It is pivotal to ensure that subjects are getting important benefits from cancer therapies by measuring HRQoL directly and accurately.[31] Given that both sleep disorder and frailty are modifiable, we suppose that these contributing factors may serve as targets for remediation with potential effects on improving HRQoL. Third, this study demonstrates the association between detrimental impact and EQ-5D utility index. Of note, it is difficult to compare the original EQ-5D profile among a distinct population, probably due to significant variations with regard to sociodemographic differences, including age, race, and education level. Finally, we elected to use EQ-5D rather than other generic or disease-specific questionnaires, because it is readily available and short enough to be applied as an addition to other routine measurements, such as clinical and treatment data, while preserving the nature of a validated and standardized instrument.[32] This is particularly relevant in daily practice with a remarkable work load on critical patients, such as patients with decompensated cirrhosis in this study. Actually, Ufere et al. clearly stated that 91% of cirrhosis providers

noted competing demands for time as a marked barrier to engaging in palliative care.[33]

In conclusion, our results show that more than half of patients with decompensated cirrhosis represent impairment in HRQoL according to the EQ-5D. In addition, sleep disturbance and frailty are valuable contributors related to poor patient-reported quality of life. Moreover, pain and anxiety/depression are the most frequently affected HRQoL domains even in patients without sleep disturbance or frailty. It is imperative to timely intervene with these symptoms and deliver tailored health care.

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